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6. AUTHOR(S)
JAMES S. SCHWABER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
DEPARTMENT OF NEUROSCIENCE
UNIVERSITY OF PENNSYLVANIA
STEMMLER HALL 215
PHILADELPHIA, PA 19104-6074

8. PERFORMING ORGANIZATION REPORT NUMBER
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9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
AFOSR/NM
110 DUNCAN AVE, SUITE B115
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13. ABSTRACT *(Maximum 200 words)*
We have developed computational models of biological neural mechanisms that provide the genesis and control of network oscillations, specific patterns of oscillation, and the control of different phases in the patterns. These models are built up across several levels of biological complexity theory, beginning with individual ionic channel kinetics and ending in whole system behavior, and are grounded in accurate biological detail at every level. A major contribution of these models in in the area of complexity theory, since it is possible to observe in simulation by which the interactions in these biological nonlinear dynamic systems produce emergent properties which a re greater than the sum of their parts. The understanding of the interactions is leading to the ability to manipulate the behavior of these nonlinear dynamics systems. In some models each neuron class is represented by a population 25 neurons, and manipulation of these networks is leading to important insights in the area of biological parallel processing. All of these results are finding interest for applications within process technology and process control, as algorithms or as inspiration for novel approaches to nonlinear control problems.

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James S. Schwaber
Department of Neuroscience
University of Pennsylvania
Stemmler Hall 215
Philadelphia, PA 19104-6074
302-695-7136
302-695-8901 (FAX)
schwaber@EPLRX7.ES.dupont.com

OBJECTIVES

This work is in the area of biological neural networks, or bio-control. Our work has focused on Neural Control research that discovers and applies knowledge of biological process control to improvement of process technology and control. This program is a cross-disciplinary collaborative effort in which we pursue the opportunities, growing out of neural computation and computational neuroscience, to reverse engineer biological processes for their control principles and mechanisms. Many of these principles and mechanisms are novel and attractive from an engineering control perspective. The problems of nonlinear control are similar in kind to those "solved" by bio-control systems: they are nonlinear, dynamical, multivariate (multiple input multiple output, or MIMO). Thus, our aim is to discover and model the kinds of MIMO, dynamical and adaptive control strategies seen in bio-control.

STATUS OF EFFORT

We have developed computational models of biological neural mechanisms that provide the genesis and control of network oscillations, specific patterns of oscillation, and the control of different phases in the patterns. These models are built up across several levels of biological complexity, beginning with individual ionic channel kinetics and ending in whole system behavior, and are grounded in accurate biological detail at every level. A major contribution of these models is in the area of complexity theory, since it is possible to observe in simulation by which the interactions in these biological nonlinear dynamic systems produce emergent properties which are greater than the sum of their parts. The understanding of the interactions is leading to the ability to manipulate the behavior of these nonlinear dynamical systems. In some models each neuron class is represented by a population of 25 neurons, and manipulation of these networks is leading to important insights in the area of biological parallel processing. All of these results are finding interest for application within process technology and process control, as algorithms or as inspiration for novel approaches to nonlinear control problems.

ACCOMPLISHMENTS/NEW FINDINGS

We have performed work: (i) to develop computational models of neural mechanisms that provide the genesis and control of both respiratory oscillations and specific patterns of respiratory neurons, and (ii) to understand the mechanisms of integration and specific roles of intrinsic properties of respiratory neurons, network properties of their interconnections, and effects of afferent feedback in the genesis and control of the respiratory pattern. The models of single respiratory neurons were developed in the Hodgkin-Huxley style employing both physiological and biophysical data obtained from different medullary respiratory neurons in mammals. The neuron models include sodium and a series of potassium and calcium channels and produce the specific firing patterns of respiratory neurons recorded experimentally (i.e. adapting and ramping bursts).

Several models of the central respiratory pattern generator (CRPG) were developed. Each CRPG model includes a network of respiratory neurons with different intrinsic properties and peripheral feedback from pulmonary stretch receptors (PSR). The CRPG models differ by the respiratory neuron types and the expiratory off-switching mechanism.All CRPG models demonstrate both a stable respiratory rhythm and specific patterns of respiratory neuronal discharges. They also show a number of plausible (consistent with experimental data) alternations of the respiratory rhythm and pattern under conditions of different perturbations applied to the main afferent nerves. The
simulation of CRPG model performances under conditions of stimulation applied to PSR feedback and different afferent nerves was used for comparable analysis of the models. Using our CRPG models we also investigate the roles of intrinsic membrane properties of respiratory neurons in the control of the duration of respiratory phases and switching between them. The results of our computer simulation provide insight into the synergism of cellular, network and systems mechanisms providing the genesis and control of the respiratory rhythm and pattern.

We have developed models of parallel processing in neuronal populations. These models display the robust, stabilizing functions of processing in biological mechanisms, appear significant from a control perspective, and are being developed for application. We developed sensor fusion algorithms inspired by biological sensory integration and we are working with engineers in implementing these applications. We also investigated a hierarchical control scheme reflecting the distributed control used in the bio-control system that appears to have a stabilizing kind of feedback.

PERSONNEL SUPPORTED

First author of this work: Dr. Ilya Rybak - partially supported by AFOSR
Associated with the effort: Dr. James Schwaber, PI
Michael Ramaker, Graduate Student
Dr. Babatunde Ogunnaike, Control Engineer
Dr. Yuris Fuentes, Control Engineer
Dr. Martin Pottmann, Control Engineer

PUBLICATIONS

I.A. Rybak and J.S. Schwaber (1994) Comparative modeling of neurogenesis of the three-phase respiratory rhythm. In Proc. of Computational Neuroscience Conference (CNS'94), 83.

Kwatra H, Doyle III F, Rybak I and Schwaber, JS. A neuro-mimetic baroreceptor dynamic scheduling algorithm for cardiovascular control: analysis and applications. Neural Computation, in press.

Rybak, IA, Paton, JFRP and Schwaber, JS. Modeling neural mechanisms for genesis of respiratory rhythm and pattern I. Models of respiratory neurons, The Journal of Neurophysiology, accepted, in revision.

Rybak, IA, Paton, JFRP and Schwaber, JS. Modeling neural mechanisms for genesis of respiratory rhythm and pattern. II. Network models of the central respiratory patterngenerator, The Journal of Neurophysiology, accepted, in revision.

Rybak, IA, Paton, JFRP and Schwaber, JS. Modeling neural mechanisms for genesis of respiratory rhythm and pattern. III. Comparison of model performances during afferent nerve stimulation, The Journal of Neurophysiology, accepted, in revision.

Doyle, FJ, Rybak, IA, Ogunnaike,BA and Schwaber.JS. Neuronal modeling of the baroreceptor reflex with applications in process modeling and control. Progress in Neural Networks, special volume on Biological Neural Networks for Control, in press.

INTERACTIONS/TRANSITIONS

Participation/Presentations At Meetings, Conferences, Seminars, Etc

J.S. Schwaber and I.A. Rybak (1994) Modeling of the three-phase respiratory rhythm generation. In Proc. of World Congress on Neural Networks, (WCNN'94). San Diego, CA, Vol. 2, 744-749.

I.A. Rybak and J.S. Schwaber (1994) Computational model of network-based respiratory rhythm generation. In Proc. of the IFAC Symposium "Modeling and Control in Biomedical Systems", Galveston, TX, 554-555.

I.A. Rybak, J.F.R. Paton and J.S. Schwaber (1995) Modeling and analysis of some neural mechanisms for the genesis and control of respiratory pattern. In "From Natural to Artificial Neural Computation". Proc. of International Workshop on Artificial Neural Networks (IWANN'95) Malaga, Spain, 100-107.

I.A. Rybak, M. Pottmann, B.A. Ogunnaike and J.S. Schwaber (1995) A closed-loop model of the respiratory control system. In Proc. of the American Control Conference (ACC'95) Seattle, WA,

J.S. Schwaber and I.A. Rybak (1995) Neuronal dynamics defined by interacting membrane conductances. In Proc. of the conf. "Cortical Dynamics in Jerusalem" Jerusalem, 1995, 71.

I. Rybak, J.F.R. Paton and J.S. Schwaber (1995) Modeling of neural mechanisms for respiratory pattern generation. In Abstracts of 25th Annual Meeting of American Society for Neuroscience, Vol.21 part 3, p. 1879, pef. 737.8

I.A. Rybak, J.F.R. Paton and J.S. Schwaber. Synergism of cellular and network mechanisms in respiratory pattern generation. Proc. of Computational Neuroscience Conference (CNS'96) (submitted).

I.A. Rybak, J.F.R. Paton and J.S. Schwaber. Modeling neural mechanisms for respiratory rhythmogenesis. Proc. of APS Conf. "Neural Control of Breathing; Molecular to Organismal Perspectives" .

Consultative And Advisory Functions To Other Laboratories And Agencies

July, 1996 - JASONS Briefing, La Jolla, CA, DOD consultants
July, 1996 - ONR Neuromorphic Control Reporting, Boston, MA
January, 1994 - Dept. of Energy Symposium on Role of the National Labs in Biotechnology

Transitions

DuPont Company, Process Control - see list of investigators. The control engineers are DuPont employees.

NEW DISCOVERIES, INVENTIONS, OR PATENT DISCLOSURES

None.

HONORS/AWARDS